

Frog awareness - tidy

Welsh use of the English word 'tidy' is hard to capture. It might be defined as a job well done. Years ago some Welsh GPs used the phrase 'like frogs in a jam-jar' to explain their feelings about centralist diktats, dropped into the jam-jar on top of the frogs. Like 'tidy', 'frogs in a jam-jar', even said without a Welsh accent, is evocative.

Bandolier has long been curious about social policy, believing cynically that academics of that ilk were able to spend longer in the bath than the rest of us. Social policies are rarely examined as closely as medical decisions. The frogs, you see, are under pressure, and not just from the weight of central diktats. The *Bandolier* school of social policy has an axiom, that those frogs at the coal-face who are humanly and legally responsible for their medical decisions will croak loudly (we hope) if they don't agree with diktats.

Bandolier has stressed repeatedly the important of vigour and quality in assessing evidence, and how that evidence can only ever be a guide, because in the end it is the poor frogs who have to make the coal-face decisions. Yes, the evidence should be their guide, but our frogs must be free to make choices for decisions for which they are held liable.

We all advocate 'baby' aspirin to prevent further problems after myocardial infarction. Never mind that we are a bit woolly about the minimum effective dose, but we should be aware that there is a finite risk of gastrointestinal bleeding even at our (woolly) baby dose (*Bandolier* 86). Three hundred people at low risk have to take the baby aspirin for one to avoid a further cardiac problem net of major bleeds. Similar issues arise over anticoagulation for atrial fibrillation (more on this on the *Bandolier* Internet site).

The problems increasingly are like this: at the end of a Friday surgery (when all the patients were over 80), the last patient (also over 80) has AF. What are the pros and cons of using warfarin in a frail elderly person tenuously hanging on to an independent existence? And what takes precedence in the balancing act of treating AF, hypertension and arthritis? Don't forget that musculoskeletal conditions impact greatest on quality of life (*Bandolier* 83).

That's why we need intelligent frogs at the coal-face, and not passive implementation, because each patients is unique, and the way they and their carers judge each situation. Coal faces are difficult to see from ivory towers and other high places. A sub-title for good evidence might be as the last bastion of frogs against diktat.



TAMOXIFEN FOR

EARLY BREAST CANCER

Bandolier was asked to nominate and précis some of the great systematic reviews and meta-analyses. The papers may be famous but few people actually know the results. That's not easy, because great systematic reviews and meta-analyses will often be large, and detailed, and resistant to précis. But, for our sins, we've decided to have a try at one of the great meta-analyses, that investigating the use of tamoxifen for early breast cancer [1].

Background

Early breast cancer is when all detectable cancer is restricted to the breast or local lymph nodes (node positive cancer). Undetected disease may be present, of course, and these micrometastases might develop into new cancers in the same breast, the contralateral breast, or at distant sites. Tamoxifen is known to have some effect on reducing the rate of recurrence. The details of for how long tamoxifen needs to be taken to have the best effect, in what types of cancer it has the best effects, and the relationship between benefit through reduced recurrence of breast cancer and adverse consequences like higher rates of endometrial cancer require meta-analysis.

Review

This review sought information on all trials in early breast cancer begun before 1990 comparing adjuvant tamoxifen versus no such treatment. Trials were divided into three categories of average duration of tamoxifen use, of one, two and more than two years. Information on each individual woman, on age, menopausal status, tumour spread to nodes, and results of any oestrogen receptor measurements on the primary tumour were obtained, as well as treatment details and information on outcomes of recurrence and

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The views expressed in Bandolier are those of the authors, and are not necessarily those of the NHSE

Figure 1: Recurrence as first event in women with oestrogen receptor positive tumour

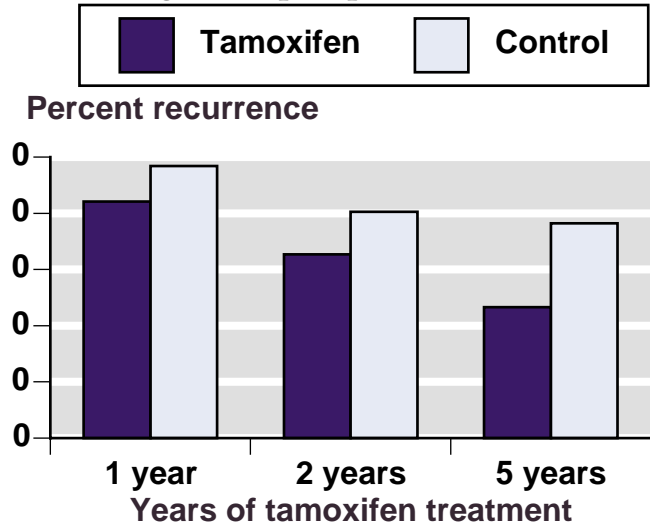


Figure 2: Recurrence as first event in women with oestrogen receptor negative tumour

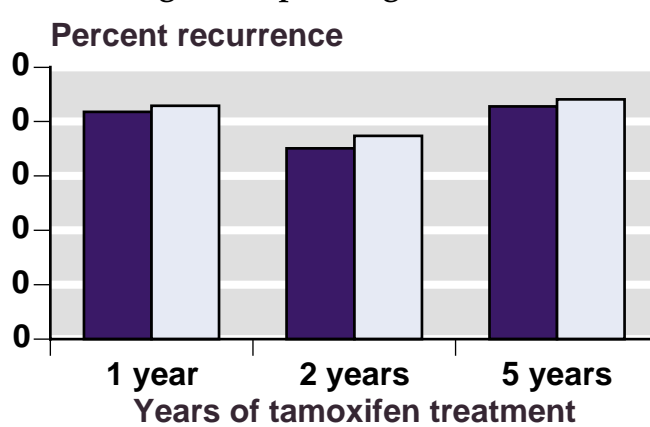
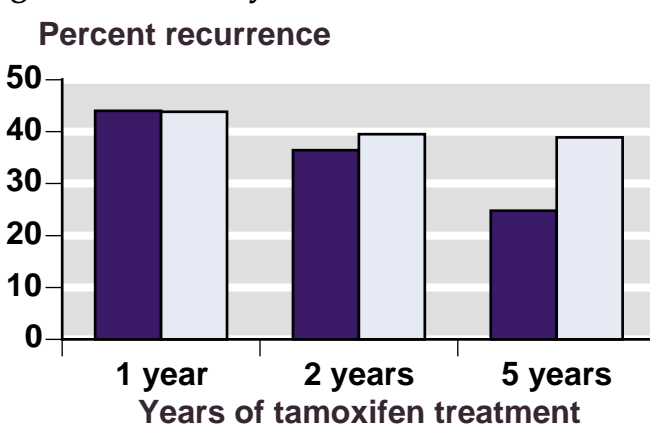


Figure 3: Recurrence as first event in women aged less than 50 years



mortality. It is unlikely that randomised trials were conducted but not included, and the analysis was by individual patient data, rather than pooling mean data from individual trials.

Results

There were 63 trials identified, and information from 55 of them, with nearly 37,000 women was available for analysis. Fourteen trials (9,000 women) examined one year duration of tamoxifen, 32 trials (19,000 women) two years, and nine trials (8,000 women) more than two years duration, with a median of five years.

Duration and oestrogen receptor status

In women with oestrogen receptor-poor tumours, tamoxifen was not effective for any duration for recurrence (Figure 1) or mortality. For women who were oestrogen receptor positive longer duration of tamoxifen produced bigger benefits in reduced recurrence (Figure 2) and mortality. Results for recurrence as first event and mortality were broadly similar in magnitude and effect of tamoxifen.

Nodal status

Tamoxifen was equally effective for women who were node negative as for those who were node positive.

Duration of effect

Benefits in recurrence were apparent early on, within the first year. After five years there was no further divergence. Benefits in mortality were not apparent in the early years, but appeared to continue to increase at least up to 10 years of follow up.

Dose

The dose of tamoxifen used is usually 20 mg, or 30-40 mg. There was no difference in results with different doses.

Age

Tamoxifen was effective in all women over 50 years. Women under 50 years receiving five years of treatment benefited (Figure 3), but there was less benefit for women under 50 with two years, and especially one year, of tamoxifen.

Benefits versus harm

Table 1 lists the benefits in terms of recurrence and death over 10 years for 1000 women who were oestrogen receptor and node positive. It also shows the effects in terms of contralateral breast cancer, colorectal cancer, endometrial cancer and endometrial cancer death, plus death from any cause other than breast or endometrial cancer. Clearly the benefits greatly outweigh the harm.

Comments

No précis can convey the wealth of detail in this meta-analysis, detail that can be used to deliver the best care to women with early breast cancer. There is little doubt, though, that these analyses point the way to even better treatment for women with breast cancer.

It demonstrated that measuring oestrogen receptor status of the primary tumour is critical because it determines optimal treatment. It demonstrated that longer duration treatment with tamoxifen provides better results, especially in women under 50. It demonstrated the benefits for women with node negative disease as well as those with node positive disease. And it demonstrated the overwhelming balance in favour of benefit over harm. It's just a shame that one woman in five is unable to use tamoxifen.

Table 1: Benefits of five years of tamoxifen treatment in women with oestrogen positive tumour and who were node positive, compared with other outcomes

Event	Number of women out of 1000 affected over 10 years		
	Tamoxifen	Control	Difference
Oestrogen receptor and node positive women treated with five years of tamoxifen			
Recurrence as first event	403	555	152
Death	386	495	109
Contralateral breast cancer	23	32	9
Colorectal cancer	7	7	0
Endometrial cancer	6	2	-4
Endometrial cancer death	1.7	0.4	-1
Death from any cause other than breast or endometrial cancer	59	59	0

What is better is that a few years from now we will have an updated meta-analysis, likely to include information on a further 6,000 women, many with longer duration of tamoxifen use.

Reference:

- 1 Early Breast Cancer Trialists' Collaborative Group. Tamoxifen for early breast cancer: an overview of the randomised trials. Lancet 1998 351: 1451-1467.

ASPIRIN AND CATARACTS

Doctor, is it right that taking an aspirin a day prevents cataracts? Interesting question, but is there an informative and authoritative answer? A new long-term analysis [1] suggests that it does not. The trouble is that previous randomised trials of aspirin for heart disease have also looked at cataract, but only over a relatively short time of five or six years. Some [2,3] suggest no effect, while an early analysis from this same trial [4] suggested some protective effect.

Study

The study was a randomised trial of 325 mg daily aspirin plus 50 mg beta-carotene in 22,000 US male doctors aged 40 to 84 years in 1982. In 1988 the aspirin component was stopped because of a significant effect on risk of a first heart attack, but the study continued with beta-carotene, when the average length of follow up was five years.

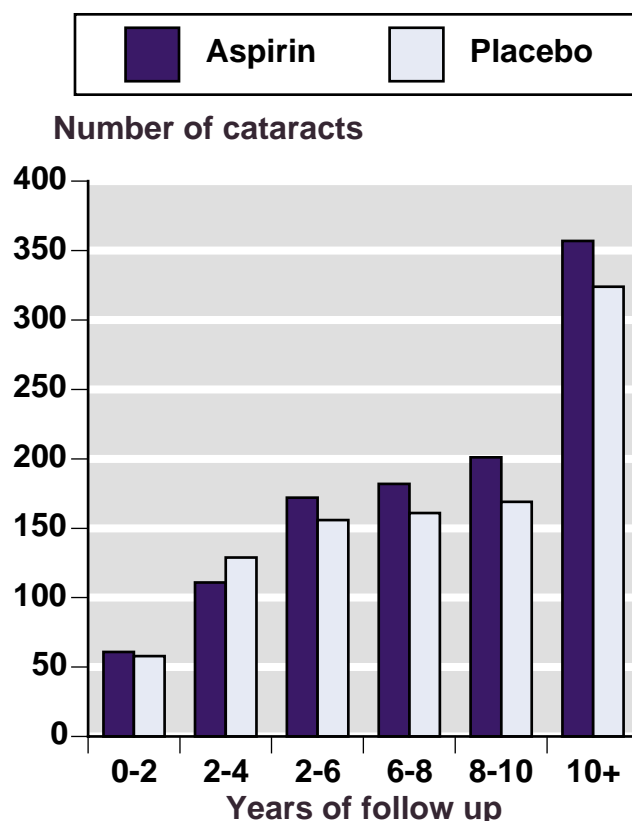
All cataracts reported up to the end of 1997, with a mean follow up of 15 years form the basis of the study. It is analysed by aspirin use during the randomised aspirin phase (intention-to-treat), and by self-reported aspirin use when doctors were given a free choice about aspirin in the sixth and seventh year of the study. Self-reported cataracts were confirmed, and details and sub types obtained from the treating ophthalmologist, with 92% confirmation.

Results

Over the 15 years the 22,071 doctors, with a mean age of 50 years in 1982, developed 2081 cataracts of which 1198 were extracted. That means that one cataract can be expected for every 10 doctors. There were 1084 cataracts in the aspirin group and 997 in the placebo group. Cataract development increased with duration of follow up, but there were no significant differences between groups (Figure 1).

In the observational analysis according to self-reported aspirin use in the sixth and seventh year, cataract development was significantly higher in doctors using aspirin for more than 180 days a year compared with those who seldom or never used aspirin (relative risk 1.22 (1.04 to 1.43). Doctors who used aspirin more tended to be older and have more heart disease, but the relationship remained the same even after adjustment for age, therapy and other factors.

Figure 1: Cataracts in US male physicians given aspirin or placebo for five years



Comment

What we can take from this and previous studies showing no association between aspirin and cataract prevention [2,3] is that it is a racing certainty that there is no large or useful effect of aspirin on preventing cataracts. Perhaps the pendulum has swung towards a suspicion that aspirin could even cause cataracts, though that is no more than a preliminary finding. For aficionados, there is a randomised study underway in 40,000 postmenopausal US doctors collecting even more information.

References:

- 1 WG Christens et al. Aspirin use and risk of cataract in posttrial follow-up of physicians health study I. Archives of Ophthalmology 2001 119: 405-412.
- 2 R Pet et al. Randomized trial of prophylactic daily aspirin in British male doctors. BMJ 1988 296: 313-316.
- 3 EY Chew et al. Aspirin effects on the development of cataract in patients with diabetes mellitus: early treatment diabetic retinopathy study report 16. Archives of Ophthalmology 1992 110: 339-342.
- 4 WG Christen et al. Low-dose aspirin and risks of cataract and subtypes in a randomised trial of US physicians. Ophthalmol Epidemiol 1998 5: 133-142.

BETA-SITOSTEROL FOR BENIGN PROSTATIC HYPERPLASIA

Suppose you are an advisor to an active local group of Age Concern that comes to you with the question of whether β -sitosterol is worthwhile for treating benign prostatic hyperplasia. After a mild panic, you have to admit that you've never heard of β -sitosterol, but you'll have quick look to see whether there's anything in the literature.

A quick search of PubMed tells you that there's a recent systematic review [1], and what's more you can download it from the Internet. Now the real problems start, because you have to interpret this for some bright, interested, and concerned people. What can you usefully say?

Review

Immediate confidence comes from the review itself. It comes from a specialist prostate group at the Veterans Association in the USA. It uses extensive searching, including specialist databases of herbal medicines, and the Cochrane Library, and Cochrane Prostate and Complementary Medicine organisations. So it might be supposed that this is a comprehensive search.

Then the inclusion criteria are specific. Only properly randomised trials were acceptable, and the authors show they were aware of pitfalls from improper randomisation, which can give rise to falsely optimistic results. The diagnosis of benign prostatic hyperplasia has to be by recognised symptom scoring, and what constitutes β -sitosterol is clearly defined.

The outcomes are clearly defined. Symptom scoring is most important, with maximum urinary flow rate and residual volume and prostate size as secondary outcomes. The methods of analysis tell us that the reviewers know how to deal with difficult issues like incomplete reporting of continuous data (for instance where no standard deviations or errors are given with continuous data).

Results

The first problem is that there were only four randomised trials with 519 men randomised. The second is that they all used different β -sitosterol preparations. The third is that while three had lasted six months, one was of only four weeks. Given these problems, was there any benefit?

Three studies reported symptom scoring, and all showed significant benefits for β -sitosterol over placebo. Three of four also showed significant benefits for peak urinary flow rate and three for residual volume. The study consistently showing no benefit was the smallest of the four.

Comment

Now comes the difficult bit: giving some advice to these bright older folk from Age Concern. There is a variety of problems you need to convey.

The problems are that β -sitosterol comes in many different forms and there is simply no guarantee that anything used resembles any of the products in the trials. The review discusses the bewildering mixture of phytopharmacological extracts that can form β -sitosterol, including whether or not the β -sitosterol is glucuronidated or not. No mechanism of action is known, and there is no basic science to fall back on to help in evaluating the results.

There is some evidence of benefit, but there is still the possibility of residual bias. We are told about randomisation, but not about double blinding. Unblinded studies can give falsely optimistic results. The numbers are pitifully small, with only 440 men studied for at least six months. There is no information given about possible harm, or interaction with other medicines likely to be taken by older people.

None of the studies compared β -sitosterol with conventional pharmaceuticals. That means we just don't know how treatments compare. All the review tells us is that in two of the trials men had only moderately inconvenient symptoms.

So, much as it would be nice to be positive about this, the best we can manage is to advise caution. *Caveat emptor*. Ask the vendors for full information. Ask the vendors about possible harm. Ask the vendors how much they are spending on research and development to help answer these questions.

Reference:

- 1 TJ Wilt et al. β -sitosterol for the treatment of benign prostatic hyperplasia: a systematic review. BJU International 1999 83: 976-983.

ERYTHROPOIETIN FOR ANAEMIA WITH CANCER THERAPY

Individuals with cancer commonly have anaemia because of changes in the production of erythropoietin caused by the cancer or its treatment. When haemoglobin levels fall, the anaemia may be treated by transfusion. There can be problems with this, because blood supplies are often limited, and because increasingly we are aware of infections from transfusion. Treatment of blood for transfusion is increasingly complicated and expensive.

So can treatment with exogenous erythropoietin reduce the need for transfusion associated with cancer or cancer treatment? A new systematic review suggests that it can [1], and also demonstrates good standards of systematic review in an awfully difficult area.

Review

Controlled trials, including randomised studies and nonrandomised studies with concurrent or historical controls were used, but the latter had to show comparability between groups. In the event only a few of these were found, and largely not used for analysis. Included studies had to enrol patients with existing anaemia because of chemotherapy or radiotherapy, or have nonanaemic patients beginning a course of therapy.

The main outcome sought was transfusion, though others, including quality of life, were examined. Higher quality randomised trials were defined as those that were both randomised and double blind, with intention to treat analysis and with fewer than 10% patient exclusions.

Results

There were 18 randomised trials with 1,700 patients, about half in adults with haemoglobin levels less than 100 g/L. There were three trials enrolling 108 children with haemoglobin less than 100 g/L.

Fourteen adult trials reported on transfusions, and all found that fewer patients were transfused with erythropoietin. For seven of twelve studies with sufficient data for computation of odds ratios there was a statistical difference between erythropoietin and control. Without erythropoietin, and with initial haemoglobin below 100 g/L, between 36% and 69% of patients were transfused. With erythropoietin be-

tween 20 and 53% were transfused. The range of differences in individual trials was 9% to 45%. Similar results were found in the three trials enrolling children and with adults with higher initial haemoglobin levels.

Odds ratios and numbers needed to treat were given (Table 1). In twelve randomised trials the number needed to treat to prevent one transfusion was 4.4. It was 5.2 in higher quality trials and 2.6 in lower quality trials. Confidence intervals did not overlap, and this probably just achieved statistical significance.

Comment

This study is interesting because of its detail as well as its result, and because it highlights an important area in cancer and palliative therapy. There is information on number of units transfused (the range of savings is 0 to 1.3 units a month for all adults, and 1.1 to 2.2 units a month for children), and on some quality of life outcomes, though there was little information on the latter.

Though methodologically sound, the systematic review falls down on one thing: it fails to give us details plus results of the individual studies. This means that if we have other ideas about how data may be analysed, we have to get all the papers and start again. That's not always a bad thing, but irritates because we cannot do a quick check of the results.

It is another example of the importance of minimising bias. For instance, in studies that were not blinded, a knowledge of treatment actually received could influence clinical decisions about the necessity for a transfusion. That may be one reason why higher quality studies had a lower estimate of efficacy than lower quality studies. Pooling information from all studies without some sensitivity analysis can never be safe, and we have to wonder why we still have to bang on about it. In any event, here the lesson is learned again.

Erythropoietin does not come cheap, though. The estimated US cost per chemotherapy cycle is given as US\$3,700 to \$6,600. The evidence on efficacy needs to be balanced against this. There is some interesting work for someone on cost-effectiveness, and on trials that describe more fully beneficial effects on quality of life.

References:

- 1 J Seidenfeld et al. Epoetin treatment of anemia associated with cancer therapy: a systematic review and meta-analysis of controlled clinical trials. Journal of the National Cancer Institute 2001 93: 1204-1214.

Table 1: Erythropoietin for anaemia - effect of quality of study on efficacy measure

Type of study	Number of studies	Odds ratio (95%CI)	NNT (95%CI)
All randomised	12	0.4 (0.3 to 0.5)	4.4 (3.6 to 6.1)
Higher quality	5	0.5 (0.3 to 0.6)	5.2 (3.8 to 8.4)
Lower quality	7	0.1 (0.06 to 0.3)	2.6 (2.1 to 3.8)

Outcome was avoidance of transfusion
Subcutaneous EPO was 300-450 units/kg/week

EBM IN GENERAL PRACTICE

Bandolier XX pointed to work examining how evidence-based medicine was regarded and used in Wessex in 1996. We now have an update from Sydney in 1999 [1]. Different continent, similar results, and some important messages.

Evidence based practice is usually put into the context of *framing* a question, *locating* evidence, *appraising* the evidence, *applying* the evidence and then *evaluating* performance. Fine ideals, but a tad difficult on a wet Tuesday in Grimsby in the middle of a 'flu epidemic. General practitioners might be forgiven for a healthy degree of scepticism: the magic is that so many of them enthuse about the use of evidence despite the numerous obstacles they face.

Study

The new study was conducted among 60 GPs in Sydney in mid-1999. It used generally similar methods and questions as the previous Wessex survey [2], but with additional questions. Sixty GPs participated, and all returned their questionnaires.

Results

Access and understanding

Two-thirds of GPs had access to the Internet at home or work, but only 8% had access to the Cochrane Library. Australian GPs were generally favourably inclined towards evidence-based medicine, but knowledge of technical terms to the level of being able to explain them to others was low. Only one in five had the confidence to do this for systematic review and one in ten for confidence interval. By contrast for most technical terms between a third and a half of GPs admitted to not understanding them, but wanting to.

Barriers to EBM

Important barriers to the use of evidence-based medicine were four: unrealistic patient expectations, time, skills and money.

The largest single barrier, noted by almost half these Australian GPs, was that patients demand treatment despite a lack of evidence of effectiveness, and one GP in five was concerned about unrealistic patient expectations driving treatment choice, rather than the evidence.

Time was a huge problem, whether for locating, reading and appraising evidence, or for discussing the evidence with patients. One in four GPs was worried about the cost of purchasing resources for evidence-based practice, and lack of skills was important to a minority of GPs.

Useful resources

Clearly top were evidence-based clinical practice guidelines, and journals summarising important research evidence, like Evidence-based Medicine and *Bandolier*. Systematic re-

Access and understanding

Internet access for 67%
Low understanding of EBM terms
Huge demand for more education

Barriers to EBM

Unrealistic patient expectation and demand
Time, Money
Skills

Resources to provide

Evidence-based practice guidelines
"Evidence-based Medicine", *Bandolier*
Ongoing quality education

views, or original articles, including the Cochrane Library, were bottom of the list.

Comment

This paper carries some critical messages. The first is that any organisation wanting to support GPs has to "Get Real!" These are busy, overworked people. The will is there to use evidence-based medicine, but not the time. They need skills teaching and easily assimilated digests of evidence, preferably with quick Internet access so they can get it within three clicks when they need it. Organisations trying to force all the responsibility downwards need to know that it just won't work.

Look at it in a positive way. Organisations need to help GPs with education on evidence-based medicine skills and understanding, so they can have confidence in advice given them, from whatever source (health service, pharmaceutical company, expert opinion). Then provide them with digests - simple to read with a clinical bottom line at the top. Then put it on an Internet or intranet. We call it the Internet version of *Bandolier*, so it can be done.

There's another lesson about barriers. It's one thing to help and educate GPs, but we now have vociferous patients demanding their "rights". That might include some completely useless treatment, like homeopathy, that we know doesn't work. GPs in particular need to be protected from decisions like this (after all, which of us questions our anaesthetist?). Patients themselves must become targets for education about evidence. They will have to acknowledge the balance between a right of access to a treatment known to work, and responsibility to purchase for themselves treatments known not to work.

References:

- 1 JM Young & JE Ward. Evidence-based medicine in general practice: beliefs and barriers among Australian GPs. *Journal of Evaluation in Clinical Practice* 2001 7: 201-210.
- 2 A McColl et al. General practitioner's perceptions of the route to evidence-based medicine: a questionnaire survey. *BMJ* 1998 316: 361-365.

STENT OR PTCA FOR ACUTE MYOCARDIAL INFARCTION?

In acute myocardial infarction there is now a choice of reperfusion strategies between balloon angioplasty and the use of a stent. Which is better? A meta-analysis suggests that the use of stents leads to lower rates of target vessel revascularisation and major adverse cardiac outcomes [1].

Review

The review sought trials comparing randomised trials of primary stent implantation compared with primary balloon angioplasty for acute myocardial infarction having outcomes of interest. These outcomes were death, reinfarction, target vessel revascularisation and major adverse cardiac events (including death, reinfarction, disabling stroke and target vessel revascularisation). MEDLINE was searched to December 2000, as well as abstracts of medical meetings carried in major cardiology journals and reference lists of papers and reviews.

Outcomes had to be reported for at least six months of follow up, and for each trial results at the longest follow up were used. Investigators were contacted when results of particular outcomes were not reported.

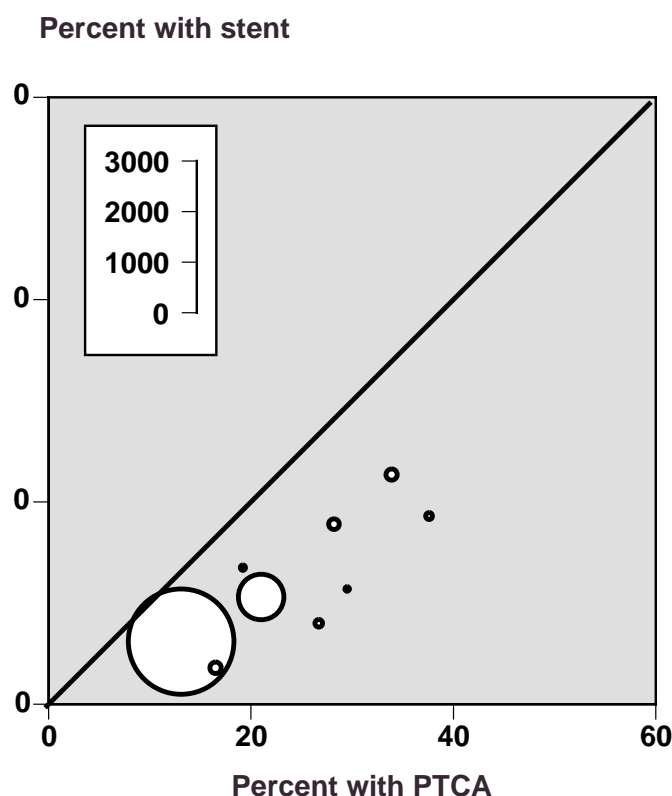
Results

There were nine included studies varying in size from 88 to 2,082 patients (4,120 in total). Five trials have yet to be published in full, but contained over half of the patient information. In all studies patients were within 24 hours of onset of symptoms, and vessel diameters were generally larger than 2.5 to 4.5 mm. Six different stents were represented, one with and one without heparin coating. Follow up was six months for about 2,400 patients.

There was no difference between procedures for death or reinfarction, occurring at about 2-4% (Table 1).

Target vessel revascularisation (Figure 1) was needed about half as often with stents (8%) as with balloon angioplasty (17%). For every eleven patients treated with a stent rather than balloon angioplasty, one fewer needed a revascularisation procedure.

Figure 1: Target vessel revascularisation needed with stents and PTCA in randomised trials



Major adverse cardiac events, including death, revascularisation, disabling stroke and target vessel revascularisation (Table 1), occurred about half as often with stents (13%) as with balloon angioplasty (23%). For every eleven patients treated with a stent rather than balloon angioplasty, one had a major adverse cardiac event.

Comment

This review packs an awful lot into very few pages, and one result is that we know precious little about the patients themselves, making it difficult to know whether they were like any patients we might treat. The low death and reinfarction rates suggest that they were at relatively low

Table 1: Outcomes in randomised trials comparing stents and PTCA in acute myocardial infarction

Outcome	Number of trials	Patients with events/total (%)		Relative risk (95%CI)	NNT (95%CI)
		Stent	PTCA		
Death	9	77/2050 (3.8)	75/2070 (3.6)	1.0 (0.8 to 1.4)	Not calculated
Reinfarction	7	40/1873 (2.1)	56/1889 (3.0)	0.7 (0.5 to 1.1)	Not calculated
Target vessel revascularisation	9	165/2050 (8.0)	352/2070 (17.0)	0.5 (0.4 to 0.6)	11 (9 to 14)
Major adverse cardiac event	8	258/1940 (13.3)	440/1958 (22.5)	0.6 (0.5 to 0.7)	11 (9 to 15)

risk. We do know they were mostly without cardiogenic shock and with cardiac anatomy suitable for stenting. Also, five trials have yet to be published in full, but contained over half of the patient information.

So these results need to be treated with a degree of caution. Even so, they represent what might be an important result for anyone designing or running a cardiac service. The lower rates of target vessel revascularisation and major adverse cardiac events, affecting about 10% of patients, suggest that stents might be a useful treatment, despite likely higher initial costs. Whether lower reinfarction or mortality might be found in patients at higher risk remains unknown.

References:

- 1 MM Zhu et al. Primary stent implantation compared with primary balloon angioplasty for acute myocardial infarction: a meta-analysis of randomized clinical trials. *American Journal of Cardiology* 2001 88: 297-301.

BOOK REVIEW

Snake Oil, John Diamond Vintage £7.99 ISBN 0099428334

John Diamond died in March 2001 three years after he was diagnosed with throat cancer. Many will have read about the progress of his disease in the Times weekly column that he wrote and in his book: *C; Because Cowards get Cancer too* (*Bandolier* 71). His fight was no different from the many courageous battles undertaken by cancer sufferers but as a journalist and broadcaster John Diamond had the skill and the opportunity to make his fight public.

During his illness he formed strong opinions about alternative therapies in cancer treatment and the first six chapters of his unfinished book, *Snake Oil* (edited after his death by his brother in law, Dominic Lawson), deal with this topic. The second half of the book contains examples of his articles both about cancer and about other subjects - the one on happiness that he wrote in Jan 2001 is just beautiful.

For a wordsmith of John Diamond's calibre it must have been particularly harsh to lose the ability to communicate verbally. It may have been some consolation to him, and certainly to the advantage of his readers, that he was able to use IT as an alternative communication tool.

Bandolier's view is that both of John Diamond's books should be standard texts, allowing his marvellous literary legacy to educate future generations.

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DAMMING HALF THE STREAM

People have enquired about the comments in *Bandolier* 90 about a report from the Boston Consulting Group that asks whether market interventions work to ensure cost-effective access to innovative pharmaceuticals, not surprisingly, sponsored by a major pharmaceutical company. The evidence it uses is somewhat different from that we are used to. Its conclusion is that market interventions have often been counterproductive.

Interventions and results

The report examines effects on supply and demand of price or volume controls to hold down costs, to limit "unnecessary" prescribing or steer prescribing to lower-cost products, or to control overall spending. One example of effects on costs in different countries is shown in Figure 1, where higher consumption is generally related to lower prices.

A very brief summary of results showed that:

- ◆ Countries with more market interventions did not have lower spending than countries with fewer interventions.
- ◆ Market interventions have substantial impacts in the shorter, but not the longer term.
- ◆ Policies limiting drug use (like limited formularies) often result in additional spending elsewhere (like hospital visits and admissions).
- ◆ More competition, like off-patent generics, drives down prices effectively.
- ◆ More market interventions result in delayed access of innovative pharmaceuticals.
- ◆ There is an increasing trend for later entrants in markets (a new PPI, for instance) to drive down prices.
- ◆ R&D investment by pharmaceutical companies is highly responsive to restrictive government interventions.

An educating read. There may be little individuals can do, but the message, as a famous economist once said, is that you "can't buck the market".

Ensuring cost-effective access to innovative pharmaceuticals. Do market interventions work? Boston Consulting Group April 1999 at www.warner-lambert.com/pricecontrolstudy/study_cover.html

Figure 1: Correlation of pharmaceutical prices and consumption in the 1990s (UK in open circle) by county

